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# Myocardial Metastases

## A Pathological and Electrocardiographic Study

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Reports differ concerning the frequency and localization of carcinomatous metastases in the myocardium as well as the different primary tumours giving rise to myocardial metastases. Series that are thoroughly investigated generally reveal a higher incidence, and Willis (1952) considers that inadequate examination is responsible for the opinion that myocardial metastases are rare.

Not all investigators distinguish between true embolic metastases and tumours invading the heart from the lung or mediastinum. In some instances pericardial metastases are included.

It is difficult to diagnose myocardial metastases by electrocardiography. Hanfling (1960) concludes, for instance, that "there are no diagnostic patterns . . .", while the New York Heart Association's 6th edition of *Nomenclature and Criteria for Diagnosis* notes concerning myocardial metastases that "electrocardiographic abnormalities, especially inversion of the T wave and persistent displacement of the S–T junction and segment, are occasionally observed in the presence of tumours in the ventricular myocardium". On the subject of pericardial metastases it is noted that "the electrocardiogram may display nonspecific abnormalities . . .". On the other hand, there is also a large number of reports on myocardial metastases diagnosed *in vivo*. An extensive review has been compiled by Hurst and Cooper (1955).

Our records contain a large homogeneous series of cases in which the pathological anatomy has been thoroughly examined. This has prompted a study of the incidence and localization of myocardial metastases for various primary tumours as well as the extent to which they could be demonstrated by electrocardiography. The retrospective nature of this material makes it difficult to assess from a purely clinical point of view.

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### Subjects and Methods

During the period 1958–65 a total of 10,160 necropsies was performed at Malmö General Hospital. It was found that 3481 of these patients had 3801 carcinomas between them, of which 2595 (68%) had metastasized.

The myocardium had been sectioned and examined macroscopically in all cases, while at least one section had also been studied histologically. Cases of continuous overgrowth to the heart are not included, neither are metastases confined to the pericardium.

The 2595 carcinomas with metastases included 122 cases involving the myocardium. Electrocardiograms were available for 37 of these 122 cases, recordings having been made less than one month before death in 25, and within 2–3 months in the other 12.

The diagnostic value of the cardiogram was tested by one of us (J.S.) examining these 37 cardiograms mixed at random with "controls" consisting of cardiograms from 41 patients from the total material of carcinomas without myocardial metastases. The age of the patients was known to the reader of the cardiograms, and the "controls" were matched as to age with the patients having myocardial metastases. The electrocardiograms were classified under three headings; *no*, *slight*, and *strong* suspicion of metastases. The examiner was therefore fully aware that roughly half of the cases had myocardial metastases, and consequently even minor changes in the curves were no doubt regarded with considerably greater suspicion than is the case with a routine analysis. Since there are no specific electrocardiographic changes generally considered to indicate myocardial metastasis, admittedly negative and non-specific criteria had to be adopted. All changes were considered including arrhythmias and QRS and ST–T abnormalities. Taking the age of the patient into account, the cardiogram was judged as indicating a suspected metastasis if there was any type of change that deviated at all from those usually regarded as characteristic of ischaemic heart disease. If ST–T abnormalities indicating pericardial involvement were present, the electrocardiogram was classified as giving suspicion of metastases.

As expected, the patients tended to be elderly, the mean age for the 37 being 69 years, and only 24 per cent of them were less than 60 years of age.

TABLE I

FREQUENCY OF MYOCARDIAL METASTASES FROM TUMOURS IN DIFFERENT ORGANS

| Location of primary tumour | Frequency of myocardial metastases among metastasizing tumours* | | | % myoc. metast. of 2595 tumours (present series) | % metast. tumours (present series) | No. of organs with metast. among metast. tumours (mean) | No. of lymph node sites with metast. among metast. tumours (mean) |
|---|---|---|---|---|---|---|---|
| | Present series | Walther (1948) | Willis (1960) | | | | |
| Melanoma (skin) | 17/33 (51·5) | 9/20 (45) | 1/4 (25) | 47 | 92 | 9 | 3 |
| Vulva | 4/8 (50) | 0/15 (0) | — | 40 | 80 | 5 | 3 |
| Melanoma (eye) | 3/9 (33) | 0/5 (0) | — | 33 | 100 | 9 | 2 |
| Hypopharynx | 1/4 (25) | 2/77 (3) | — | 14 | 57 | 2 | 2 |
| Thyroid | 6/33 (18) | 3/46 (6·5) | 2/6 (33) | 12·5 | 69 | 3 | 2 |
| Anus | 1/5 (20) | 0/4 (0) | — | 14 | 71 | 3 | 3 |
| Testes | 2/12 (17) | 1/17 (6) | — | 15 | 92 | 5 | 2 |
| Gingiva | 1/7 (14) | 1/16 (6) | — | 11 | 78 | 2 | 2 |
| Larynx | 1/7 (14) | 0/7 (0) | — | 9 | 64 | 3 | 3 |
| Kidney | 13/94 (14) | 4/53 (7·5) | 2/10 (20) | 6 | 46 | 4 | 1 |
| Ureter | 2/17 (12) | 0/1 (0) | — | 10·5 | 89·5 | 3 | 2 |
| Liver | 8/104 (8) | 1/29 (3) | — | 5 | 65 | 2 | 2 |
| Collum uteri | 5/70 (7) | 0/92 (0) | 1/30 (3)† | 6 | 85 | 3 | 3 |
| Lung | 19/357 (5) | 9/233 (4) | 3/27 (11) | 5 | 87 | 3 | 3 |
| Pancreas | 7/158 (4) | 2/56 (4) | 2/11 (18) | 4 | 95 | 3 | 2 |
| Urinary bladder | 3/75 (4) | 0/16 (0) | — | 3 | 65 | 3 | 2 |
| Small intestine | 1/26 (4) | 0/11 (0) | — | 1 | 28 | 1 | 2 |
| Mamma | 9/312 (3) | 0/134 (0) | 2/45 (4) | 3 | 94 | 4 | 5 |
| Oesophagus | 1/50 (2) | 5/219 (2) | 0/17 (0) | 2 | 79 | 2 | 2 |
| Colon, rectum | 6/333 (2) | 0/188 (0) | 0/65 (0)‡ | 1 | 67 | 2 | 2 |
| Stomach | 6/339 (2) | 6/452 (1) | 2/85 (2) | 1·5 | 86 | 2 | 3 |
| Prostate | 3/180 (2) | 1/71 (1) | 0/15 (0) | 0·4 | 26 | 2 | 3 |
| Gall-bladder | 2/130 (1·5) | 2/85 (2) | 0/18 (0) | 1 | 87 | 2 | 2 |
| Ovary | 1/119 (1) | 0/43 (0) | 0/9 (0) | 1 | 91 | 3 | 4 |
| Total | 122/2595 (5) | 46/2027 (2) | 17/342 (5) | 3 | 68 | 3 | 3 |

* Figures in parentheses are percentages.
† Uterus.
‡ Intestine.

These retrospective cases came from all departments in the hospital. The recordings for 22 of the patients unfortunately comprised only 4 leads (I, II, III, and V4). The customary 12-lead electrocardiogram was available for the other 15.

## Results

There were 122 cases (58 women, 64 men) of myocardial metastases among 2595 patients (1303 women, 1292 men) with metastasizing tumours.

The frequency of myocardial metastases from different primary tumours (only metastasizing ones) are shown in Table I (column 2), in which tumours are arranged in descending order of frequency together with the frequencies reported by Walther (1948) and Willis (1960). The last four columns give the frequency of myocardial metastases among all the tumours (even non-metastasizing) in each group, the percentage number of tumours that metastasized at all among the various primary tumours, and the degree of metastasization (the average number of lymph node stations and other organs with metastases among metastasizing tumours).

Metastases were observed macroscopically in 101 (83%) of the 122 cases and were discovered during a routine microscopical examination of a macroscopically normal myocardium in the other 21 (17%). (The microscopical examination was usually made on parts of the anterior wall of the left ventricle.)

The 101 cases with macroscopical metastases comprised 44 (44%) with solitary and 57 (56%) with multiple foci. The locations of the solitary metastases are shown in Table II.

TABLE II

MYOCARDIAL LOCATION IN CASES WITH A SOLITARY METASTASIS

| Location | No. of cases | Percentage |
|---|---|---|
| Left ventricle | 25 | 61 |
| Left atrium | 2 | |
| Right ventricle | 8 | 30 |
| Right atrium | 5 | |
| Septum | 4 | 9 |
| Total | 44 | 100 |

The multiple metastases were present in a large number of different sites. The left heart was involved in 79 per cent and the right in 56 per cent.

The necropsy findings are compared in Table III with the interpretation of electrocardiograms for all the 37 cases with myocardial metastases for which such recordings were available as well as the 41 "control" cases without myocardial metastases.

These data clearly show that the electrocardiogram, interpreted without knowing anything else

TABLE III

ELECTROCARDIOGRAPHIC ANALYSES COMPARED WITH NECROPSY FINDINGS

| Necropsy findings | Metastasization assessed from electrocardiogram* | | | |
|---|---|---|---|---|
| | No suspicion | Slight suspicion | Strong suspicion | Total |
| "Controls" | 25 (61) | 12 (29) | 4 (10) | 41 |
| Myocardial metastases | 18 (58) | 7 (23) | 6 (19) | 31 |
| Myo-pericardial metastases | 4 (67) | 1 (17) | 1 (17) | 6 |
| Total | 47 | 20 | 11 | 78 |

* Figures in parentheses are percentages.

TABLE IV

ELECTROCARDIOGRAPHIC DIAGNOSIS WITH DIFFERENT TYPES OF MYOCARDIAL METASTASES

| Necropsy | Electrocardiographic assessment | | | |
|---|---|---|---|---|
| | No suspicion | Slight suspicion | Strong suspicion | Total |
| Microscopical metastasis | 2 | 2 | 1 | 5 |
| Macroscopical metastasis | | | | |
| Solitary | 10 | 0 | 3 | 13 |
| Multiple | 10 | 6 | 3 | 19 |
| Total | 20 | 6 | 6 | 32 |

about the clinical picture, does not give the diagnosis of myocardial metastasis.

A somewhat better agreement with the necropsy findings is obtained if the comparison is confined to the 25 cases with cardiograms taken within a month of death. The records were then classed as "no suspicion" in 44 per cent and as "slight" and "strong suspicion" in 28 per cent of the cases. This comparison is probably more valid than the former one, since metastasis to the myocardium is presumably a relatively late phenomenon.

There was a large proportion of elderly people among the present cases and consequently arteriosclerotic changes may have complicated the assessment of the curves. If, however, we exclude the 10 cases in which infarction or severe coronary sclerosis was found at necropsy, the electrocardiographic assessments for the other 27 cases showed "no suspicion" in 59 per cent, "slight suspicion" in 22 per cent, and "strong suspicion" in 19 per cent, which is the same distribution as in Table III. There were 5 cases in which no coronary sclerosis could be demonstrated at necropsy, and in 2 of these metastases were suspected from the cardiogram.

The electrocardiographic assessments are compared with micro- and macroscopical metastases in Table IV. As indicated in Table III, the diagnostic accuracy of these assessments was no higher in cases with pericardial metastases than it was in pure myocardial metastasis. The difficulties in diagnosing involvement of the pericardium are illustrated by Fig. 1, which shows the cardiogram 14 days before death in a patient in whom multiple macroscopical metastases were found at necropsy in the pericardium which contained 250 ml. fluid.

Fig. 2 shows another electrocardiogram taken one day before death. The patient was a cachectic man, though without cardiac failure, and no involvement of the pericardium was found at necropsy. There was severe coronary sclerosis with apical infarction.

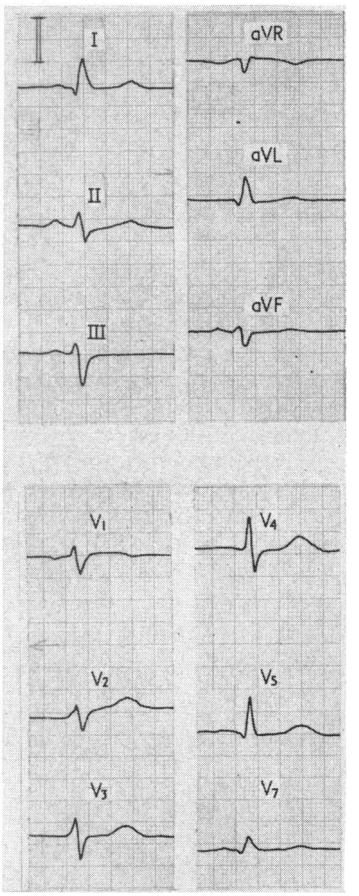


FIG. 1.—Electrocardiogram 14 days before death in a patient with multiple macroscopical pericardial metastases.

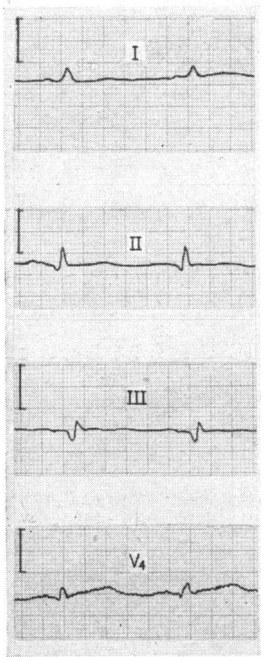


FIG. 2.—Electrocardiogram one day before death in a patient with severe coronary sclerosis and apical infarction. Multiple macroscopical metastases in the posterior wall. No pericardial involvement.

Multiple macroscopical metastases in the posterior wall from a primary hepatic carcinoma may explain the QRS changes in leads II and III.

Fig. 3 shows the cardiogram of a 42-year-old woman, recorded less than one month before death. The abnormal atrial activation, indicating an ectopic atrial focus, and the ST–T abnormalities with T wave inversion especially pronounced in V3–5, were considered to indicate, in this relatively young woman, the strong suspicion of metastatic involvement of the myocardium. The necropsy revealed thyroid cancer with microscopical myocardial metastases and phaeochromocytoma. It seems probable that the changes in the cardiogram are due to catecholamines from the phaeochromocytoma rather than to the myocardial metastases. The cardiographic picture corresponds fairly well with that presented in a similar case by Roesler and Fletcher (1963).

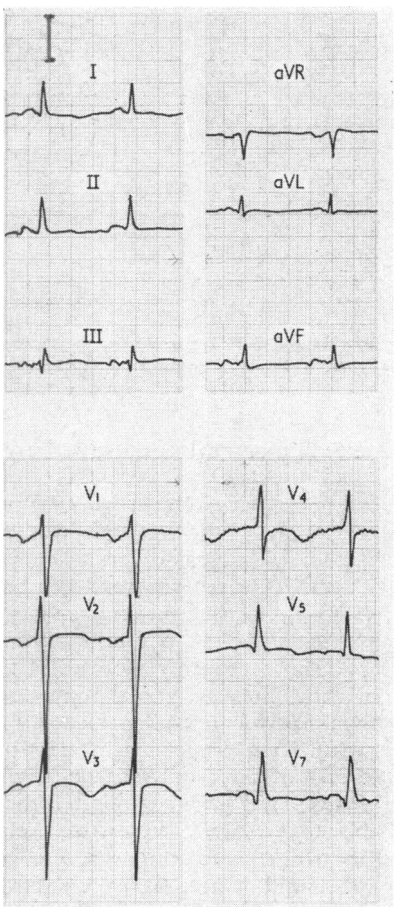


FIG. 3.—Electrocardiogram less than one month before death in a patient with thyroid cancer, microscopical myocardial metastases, and phaeochromocytoma.

TABLE V

ELECTROCARDIOGRAPHIC CHANGES CAUSING SUSPICION OF METASTASES

| Electrocardiogram | No. of cases |
|---|---|
| ST–T changes | 10 |
| with atrial fibrillation | 1 |
| with supraventr. extrasystoles | 1 |
| with low voltage | 2 |
| QRS changes | 2 |
| Low voltage | 2 |
| Deformed P and premature supraventr. extrasystoles | 1 |
| Total | 15 |

Table V shows the distribution of the various findings on electrocardiograms that prompted a suspicion of myocardial metastases in the 15 cases in which these were actually found at necropsy. The largest group of these findings comprises various degrees of ST-T abnormality. In all these cases, the abnormalities as such could in fact be interpreted as being caused by ischaemic heart disease. In the present study, however, they were taken to be suggestive of metastases even if the deviations

from customary patterns were only slight. Such deviations included, for instance, localized negative T waves, perhaps only in one or two chest leads.

The difficulties in interpreting the ST-T abnormalities are shown by the electrocardiogram of a 74-year-old woman (Fig. 4). The general ST-T changes of a slightly unusual and non-specific form were judged to indicate pericardial and/or widespread myocardial involvement. At necropsy only one macroscopical metastasis in the right ventricular wall was found without additional microscopical ones. No pericardial involvement was present, but slight coronary sclerosis and a generalized lipomatosis.

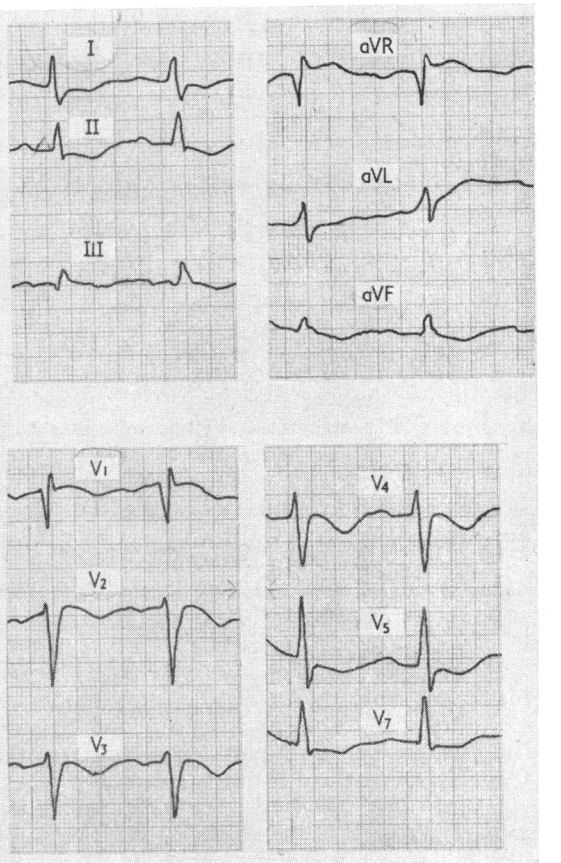


FIG. 4.—Electrocardiogram in a 74-year-old patient with only one macroscopical metastasis in the right ventricular wall. No additional microscopical metastases. No pericardial involvement.

## DISCUSSION

The varying frequencies reported for myocardial metastases, besides reflecting differences in necropsy methods and the definition of metastases, are partly due to differences in the manner of reporting. Necropsy series always represent a selection that varies with the type of hospital. A series from a hospital for chronic patients will therefore contain a greater number of cancer patients, with a preponderance of advanced cases. If microscopical examination of the prostate is performed as a routine, this will disclose a large number of tumours without metastases. The effect of this can be offset by reporting only the frequency of metastasis in various organs in relation to the number of tumours with metastases rather than to the total number of tumours. High figures will naturally be reported from hospitals specially interested in certain tumours that more frequently metastasize to the myocardium, e.g. melanoma and thyroid cancer.

Since Malmö (250,000 inhabitants) has only one hospital, the element of selection in the present series is probably less than in most other necropsy reports.

According to Morehead (1965) myocardial metastases occur in approximately 4 per cent and usually derive from mammary and pulmonary tumours as well as from melanomas. As shown in Table VI, however, very different incidences have been reported for myocardial metastases even from these sources.

Both Walther (1948) and Willis (1960) found that tumours in the kidney and thyroid frequently produced myocardial metastases. This was also the case in the present series. Here again, however, there are conflicting reports. Thus, McWhorter and Cloud (1930) found 19 per cent (including pericardial metastases) for the kidney, and 0 per cent for the thyroid, whereas Abrams, Spiro, and Goldstein (1950) found 0 per cent for the kidney, and 10 per cent for the thyroid.

It is not possible to state with certainty which factor or factors (definition of metastases, manner of reporting, selection) is chiefly responsible for these discrepancies. Furthermore, the number of tumours in different organs is so small in many series that a single case with myocardial metastasis gives a high percentage figure.

The number of metastases found is naturally liable to increase with the number of organs that are sectioned and the number of sections per organ at necropsy. It follows that negative findings say less than positive ones.

There seems to be general agreement that melanomas are responsible for the greatest number of myocardial metastases. After this come cancer of

TABLE VI

FREQUENCY OF MYOCARDIAL METASTASES IN OTHER REPORTS

| Mamma | | Lung | | Melanoma | |
|---|---|---|---|---|---|
| Author | Percentage | Author | Percentage | Author | Percentage |
| McWhorter and Cloud (1930) | 0 | McWhorter and Cloud (1930) | 0 | McWhorter and Cloud (1930) | 0 |
| Walther (1948) | 0 | Ask-Upmark (1932) | 3* | Walther (1948) | 36 |
| Abrams *et al.* (1950) | 8 | Walther (1948) | 4 | Willis (1960) | 25 |
| Willis (1960) | 4 | Abrams *et al.* (1950) | 8 | Das Gupta and Brasfield (1964) | 49 |
| Malmö | 3 | Senoo (1956) | 3–17† | Malmö | 48 |
| | | Willis (1960) | 11 | | |
| | | Warren and Gates (1964) | 10·5 | | |
| | | Malmö | 5 | | |

* Mean for 2080 tumours from 19 series.
† Range for 9 series totalling over 4000 tumours

the kidney, thyroid, and lungs, while mammary tumours lie below the mean incidence in most large series. It is probably realistic to expect a mean figure of 4–5 per cent in a thoroughly examined unselected series. In a survey of 100 previously reported cases, Willis (1952) found that 72 per cent had multiple metastases in the myocardium. His own series of 24 cases had 78 per cent with multiple tumours. In Walther's (1948) series the figure was 63 per cent and in the present series 56 per cent.

It is usually stated, even in quite recent reports, that myocardial metastases are most frequently located to the right heart (Morehead, 1965; Rabenko and Wanke, 1965). Willis (1952) considers that this is misleading and is due to "inaccurate use of the word 'metastasis', this term often having been employed to include all forms of secondary neoplastic disease of the heart, including intracardiac invasion *via* the veins, a condition which is more frequent in the right chambers than in the left". He considers that all parts of the myocardium are equivalent from the point of view of metastasis, and argues that the larger mass of musculature in the left heart is responsible for his finding of a higher percentage of metastases on this side. This opinion has also been put forward by Walther (1948). The left heart clearly predominated in the present series, too, in cases with macroscopical involvement of the myocardium. The distribution of the cases with unilateral involvement is shown in Table VII.

TABLE VII

FREQUENCY OF METASTASES IN RIGHT AND LEFT HEART AMONG CASES WITH UNILATERAL ENGAGEMENT

| Author | Right heart* | Left heart* |
|---|---|---|
| Walther (1948) | 7 (41) | 10 (59) |
| Willis (1960) | 1 (12·5) | 7 (87·5) |
| Malmö | 23 (35) | 43 (65) |

* Figures in parentheses are percentages.

It will be seen that the present figure lies between those reported by Walther (1948) and Willis (1960). Their series, particularly Willis's, were considerably smaller, and it is probably true to say that in two-thirds of cases with unilateral metastases it is the left heart that is involved.

The present results suggest that the myocardial location of metastases can be ascribed to the relative size of the blood flow and the muscle mass in the two halves of the heart. This seems to hold true only when comparing different parts of the same organ. The proportion of the total blood flow passing through different organs is, however, not correlated with the frequency of metastases. The kidneys, receiving approximately 20–25 per cent of the systemic blood flow, show 9 per cent metastases from all metastasizing cancers, compared to the frequency 19 per cent found in the adrenals.

The myocardial metastases were found among tumours with blood-borne metastases to numerous organs (cf. the right-hand column in Table I; the few exceptions concern tumours represented by only a few cases and may be due to chance). It is thus probable that myocardial metastases occur at a late stage in the disease. There is no relation, on the other hand, between the tendency of different tumours to metastasize at all and to do so in the heart (Table I, column 4). Whereas 80 per cent of the tumours in the pancreas, heart, stomach, gall-bladder, and ovaries had metastasized, less than 5 per cent had done so to the myocardium. In the upper half of the table, however, there are several tumours with a lower tendency to metastasize but a higher frequency of myocardial metastases.

The *in vivo* diagnosis of myocardial metastases was the subject of a good deal of research in the nineteen-thirties (Schnitker and Bailey, 1937). At that time it was considered that such metastases did not give a typical clinical or electrocardiographic picture. Nothing pathognomonic could be found, though cardiac findings such as arrhythmia, block,

or failure in patients known to have cancer were taken as grounds for suspecting metastasis. It has since been pointed out that metastases can give a record resembling those of infarction, and various possible mechanisms have been discussed. Queckenstedt (1956) suggested, for instance, that the ST-T abnormalities typical of recent infarction are caused by inflammatory reaction around the metastasis which itself is electrically silent, thereby producing the QRS abnormalities seen in myocardial infarction. Gassman, Meadows, and Baker (1955), on the other hand, argue that the picture can arise by the metastases disturbing the coronary circulation and thereby actually eliciting a secondary infarction. In a review of the problem, Strik, Polzien, and Maiwald (1966) state that metastasis should be suspected in cases of persistent electrocardiographic abnormalities resembling infarction, as well as in cases in which the infarction pattern lacks the reciprocal S-T depressions.

It has also been noted that metastases in the myocardium elicit various rhythm disturbances (Queckenstedt, 1956; Drouin *et al.*, 1957; Cupp, Woolvin, and Immon, 1958). It has further been pointed out that metastasis to the myocardium quite frequently involves the pericardium as well (Kruml and Widimský, 1959) which improves the chances of a diagnosis on the electrocardiogram.

There is thus no generally accepted electrocardiographic picture in cases of myocardial metastasis, and the present series provides a good illustration of this. Even though the curves were specifically analysed for changes indicative of metastasis, grounds for suspecting this were found in only 40 per cent of the 37 cases verified at necropsy. The percentage would presumably have been considerably lower at a routine interpretation of the cardiograms. The large proportion of "suspected metastasis" among the cardiograms from the control cases strengthens our conviction that the cardiogram cannot be used to diagnose myocardial metastases, except in a few favourable cases. It should, however, be emphasized that the present retrospective series unfortunately contains a large number of electrocardiograms with only four leads. Somewhat greater diagnostic accuracy may be possible with the routine use of the current 12-lead cardiogram. It is also probable that diagnostic accuracy is improved by considering the total clinical picture, of which the electrocardiogram is only a part.

## Summary

Among 122 cases of myocardial metastases, the highest frequency was found among melanomas, though cancer of the thyroid, kidney, liver, collum uteri, and lungs also frequently gave metastases to the heart.

The myocardial metastases occurred among cases with numerous blood-borne metastases and probably appeared late in the course of the disease.

The left heart was affected more frequently than the right.

An analysis of electrocardiograms taken shortly before death in 37 cases showed that no diagnostic abnormalities were present. It is considered that in most cases there is little chance of demonstrating myocardial metastases by electrocardiography alone.

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